

Obesity and fetal-maternal outcomes

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Summary

In women Obesity has a significant impact on every aspect of female reproductive life both in terms of infertility and early pregnancy complications. It is linked to a number of adverse obstetric outcomes as well as increased maternal and neonatal morbidity and mortality. These complications include miscarriage, congenital abnormalities, pre-eclampsia, gestational diabetes mellitus, iatrogenic preterm delivery, post-dates pregnancy with increased rates of induction of labour, caesarian section and complications during and following operative procedures, post-partum haemorrhage, shoulder dystocia, infection, venous thromboembolism and increased hospital day. It is important to consider obese pregnant women as a high risk group with a linear increase in risk of complications associated with their degree of obesity.

Key words: obesity, pregnancy, complications, preeclampsia

Introduction

Obesity, which is more common in females than in males, has been seen as a problem of predominantly middle-aged and older people.

The most commonly used measurement for defining of obesity is BMI (body mass index) which refers an individual's weight in kilograms divided by the square of his or her height in meters.

Individuals are deemed:

30 *overweight* when they have a BMI between 25 and 30 kg/m²;

31 *obesity* is defined as a BMI greater than or equal to 30 kg/m²,

32 *extreme obesity* is defined as a BMI greater or equal to 40 kg/m².

Obesity in pregnancy includes women who have obesity before they become pregnant and women who become obese from excess weight gain during pregnancy.

Biology of Adipose Tissue

Fat (lipid) is an essential tissue and performs multiple and diverse functions, including providing nutritional, hormonal, and even structural support. The main fat depots in the body are in adipose tissue. Adipocytes are cells specifically adapted for fat storage, serve as a future energy source, and help to avoid the negative metabolic consequences of excess cellular lipid deposits in organs such as muscle, liver, and heart. However, adipose tissue is not a passive organ. It actively regulates metabolism through multiple distinct but overlapping pathways. Adipose tissue also contains a large number of nonfat cells, including fibroblasts and immune cells such as mast cells, macrophages, and leukocytes. (1) Both adipocytes and nonfat cells synthesize and secrete numerous peptide and steroid hormones as well as cytokines and chemokines, and such factors are known to influence local and systemic physiology. (1,2) In this way, adipose tissue functions as an endocrine organ, (2) and it is the metabolic function of adipose tissue that causes much of the pathology associated with obesity. It stores and releases preformed steroid hormones, converts precursors to biologically active hormones, and converts active hormones to inactive metabolites. To this end, adipocytes express a number of enzymes critical to steroid hormone biosynthesis and metabolism. For example, estrone is converted to estradiol in peripheral adipose tissue. Indeed, most if not all circulating estradiol in postmenopausal women comes directly from adipose tissue (2). Adipose tissue expresses 11-hydroxysteroid dehydrogenase type 1 (11-HSD1), which converts cortisone to cortisol, as well as 5-reductase, which converts cortisol to 5-tetrahydrocortisol. Thus, adipose tissue regulates the local concentration of glucocorticoids and contributes to their metabolic clearance. Finally, adipose tissue secretes a large number of bioactive peptides and cytokines, collectively known as adipokines.

Complications in Obstetrics

Maternal obesity increases the risk of a number of pregnancy complications and, as such, requires adjustment to routine prenatal care.

Complications related to Body Mass Index

Obesity is associated with irregular menstruation with longer cycles, often making the expected date of delivery unsure: the vaginal examination to assess uterine size is notoriously inaccurate in overweight individuals. Also ultrasound examination of the fetus, both in terms of vaginal and especially abdominal ultrasound is more difficult in obese women and it might be more difficult to detect structural fetal abnormalities. In addition, it is technically more challenging to perform invasive prenatal diagnostic tests such as chorionic villus sampling and amniocentesis, and the risks of miscarriage are increased three-fold in the obese. In terms of amniocentesis, post-amniocentesis amniotic fluid leak and fetal loss were significantly higher in women with an increased BMI than in a control group (3).

Complications related to Obesity

Early Pregnancy

Maternal obesity is a risk factor for spontaneous abortion (for both spontaneous conceptions and conceptions achieved through assisted reproductive technology), as well as for unexplained stillbirth (intrauterine fetal demise). A recent meta-analysis revealed that obese pregnant women have an estimated risk of stillbirth that is twice that of normal weight pregnant women. (4) Several mechanisms have been proposed for this relationship, including the increased risks of hypertensive disorders and gestational diabetes that are associated with maternal obesity during pregnancy.

Late Pregnancy

Maternal obesity is associated with an increased risk of hypertensive disorders of pregnancy, including preeclampsia (gestational proteinuric hypertension), and the risk increases linearly with obesity. For each increase in BMI of 5 to 7 kg/m², there is a corresponding 2-fold increase in the risk of developing preeclampsia (5, 6). Also it is associated with an increased risk of diabetes, both pregestational diabetes and GDM (7, 8). Therefore in pregnancy there are the continued production of counterregulatory (anti-insulin) hormones by the growing placenta, and insulin resistance increases progressively throughout pregnancy. But obese women have higher insulin resistance (lower insulin sensitivity) than women of normal weight, which results in increased availability of lipids for fetal growth and development. (9)

The development of GDM has a number of adverse maternal and fetal implications. For women, these include an high risk of hyperglycemia, cesarean delivery, and diabetes in later life.

Problems in Labour

In pregnancy complicated by obesity there are at increased risk of complications at the time of labor and delivery. The rate of successful vaginal delivery decreases

progressively as maternal BMI increases. A meta-analysis of 33 studies showed that the ORs of cesarean delivery were 1.46 (95% CI, 1.34-1.60), 2.05 (95% CI, 1.86-2.27), and 2.89 (95% CI, 2.28-3.79) among overweight, obese, and severely obese women, respectively, compared with normal weight pregnant women. (10) This 2- to 3-fold increase in cesarean delivery rate is true for both primigravid and multigravid women. (11) Whether this is secondary to increased fetal size or another maternal characteristic is not known.

Also complication during operative procedures are increased. The duration of Caesarean section in the obese is longer than in control women. It can be more difficult in women with obesity to exteriorize the uterus to identify the angles and suture then to obtain haemostasis. Other technical problems can be encountered: transfer of the patient to operating tables (particularly if the woman has already had an effective epidural) and the need for special operating tables in the grossly obese.

The reason obese pregnant women are more likely to end up with a cesarean delivery is not known, but a theory is that obese women are more likely to experience dysfunctional labor. For example, Vahratian and colleagues (12) found that the rate of cervical dilation in nulliparous women in spontaneous labor decreased as maternal BMI increased. In this study, normal weight women (BMI 19.8-26.0 kg/m²) took a median duration of 5.43 hours to dilate from 4 to 10 cm, whereas obese women (BMI \geq 29.0 kg/m²) took 6.98 hours. This appears to be true also in women undergoing induction of labor at term. Although multiparous women progressed faster during induced labor than nulliparous women, in both groups an increase in maternal weight quartile was associated with a decreased rate of cervical dilation and an increase in the duration of labor (13).

There is an increased incidence of fetal macrosomia (birth weight >4 kg) in obese women and, if delivered vaginally, there is an increased risk to the woman of a third-degree tear. With regard to the fetus, trauma is more common, especially brachial plexus injuries, due in part to a higher incidence of shoulder dystocia.

Therefore a higher maternal BMI in the first trimester and a greater increase in BMI throughout pregnancy were associated with a reduced likelihood of spontaneous labor at term, an increased risk of post-term pregnancy, and rate of intrapartum complication (14).

Postoperative complications

In addition to an increased rate of operative delivery, obese women are also an high incidence of intraoperative complications, including increased infectious morbidity and thromboembolic events. There is also an increased risk of anesthetic complications, such as failed intubation at the time of general endotracheal anesthesia (15).

Infact difficulty with venous access and the increased depth of tissue to the intervertebral space make the establishment of an epidural or spinal for analgesia more difficult; thus the rate of general anaesthesia is higher. Morbidly obese women also have a higher risk of problems with general anaesthesia and a higher rate of episodes of severe hypertension. Due to the over hanging of the pannus, there are significantly increased inci-

dence of wound infection even if given postoperative prophylactic antibiotics. We would therefore recommend an interrupted suture or skin clips on the basis that if a small haematoma or a localised area of infection develops, a few clips/ sutures can be removed to aid resolution.

Also chest infection are more common in obese women possibly due to problems in early mobilisation and restricted chest movement.

An other complication more dangerous and more frequently in obese pregnant women is deep venous thrombosis/pulmonary embolism (DVT/PE). These complications are the third most common cause of maternal mortality.

To minimise these risks, patients should be given thromboembolic stockings (TEDS), which should be fitted prior to surgery and possibly used for up to 6 weeks after delivery. Also a course of subcuticular enoxiparin should be considered. The normal dose should be increased to 40 units per 24 h for 1 week and possibly for 6 weeks. Antepartum venous thromboembolism is also increased, with an adjusted odds ratio of 2.17 (95% CI 1.30–3.63) in moderate obese patients and of 4.13 (95% CI 1.25–13.54) for severely obese patients.

Finally obesity is associated with an increased instance of maternal mortality from a number of different causes. In the most recent confidential enquiries into maternal deaths, 78 (35%) of women who died from either direct or indirect causes had a BMI >30.

Effect on Prenatal Outcome

Maternal obesity is associated with abnormal fetal growth. Therefore in obese pregnant women is fetal macrosomia (defined as an estimated fetal weight of greater than or equal to 4500 g), which appears to be increased 2- to 3-fold in obese parturients with a dose-dependent relationship between maternal obesity and fetal macrosomia (16).

In this patients there are also an increased risk of neural tube defect (NTD) in the offspring. A recent meta-analysis by Rasmussen and colleagues (17) reported that the OR for delivering an infant with NTD was 1.22 (95% CI, 0.99-1.49), 1.70 (95% CI, 1.34-2.15), and 3.11 (95% CI, 1.75-5.46) among overweight, obese, and morbidly obese women, respectively, compared with normal weight women. The mechanism underlying the increased risk of NTD in maternal pregnancies obesity is unknown. It can caused by a reduction in the amount of folic acid reaching the developing embryo due to insufficient absorption and greater maternal metabolic demands, chronic hypoxia, and increased circulating levels of triglycerides, uric acid, estrogen, and insulin (due, in part, to increased insulin resistance) (18,19).

Moreover, offspring born of GDM pregnancies are more likely to develop childhood and adult obesity (OR 1.4 [95% CI, 1.2-1.6] for every 1-kg increment in birth weight) as well as type 2 diabetes mellitus (20).

Pregnancies complicated by GDM have a 4-fold increased risk of perinatal mortality, of shoulder dystocia and resultant birth injury (21) and Low APGAR scores, more admissions to neonatal intensive care units; and higher rates of prenatal death (22).

Conclusion

The incidence of maternal obesity continues to increase, especially in younger age group, at an alarming rate, with major public health implications. The obesity epidemic is of great concern in terms of morbidity and also for the resource, indeed Obesity costs too much and it was estimated that the cost is increased five-fold compared to women who are non-obese. (23)

Despite improvements in our understanding of this endocrinopathy, there are still many barriers to the clinical care for such women.

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